

**DOCKET NO.: ALLE0031-102  
(16952 CON1-DIV11)**

**PATENT**

**REMARKS**

Upon entry of this response, claims 18, 21-29 will be pending in this application. Amended claims 18, 26 and 29 are fully supported by the specification at, for example, page 9, lines 25-32.

**NO DOUBLE PATENTING**

Claims 18 and 21-29 are rejected under the judicially created doctrine of obviousness-type double patenting over the following U.S. Patents (referred to herein as Patents A-F):

(A) 6,887,476: filed June 18, 2001 and is a divisional of application Ser. No. 09/490,756, filed January 24, 2000, now issued, which is a divisional of Ser. No. 08/627,118, filed April 3, 1996, pending, which is a continuation of Ser. No. 08/173,996, filed December 28, 1993, now abandoned.

(B) 6,113,915: filed October 12, 1999.

(C) 6,235,289: filed May 25, 2000 and is a continuation of application Ser. No. 09/417,195, filed October 12, 1999.

(D) 6,333,037: filed May 25, 2000 and is a divisional application of serial number 09/417,195, filed October 12, 1999.

(E) 6,372,226: filed March 1, 2001 and is a continuation of Ser. No. 09/578,097, filed May 25, 2000, now U.S. Pat. No. 6,235,289, which is a continuation of Ser. No. 09/417,195, filed Oct. 12, 1999, now U.S. Pat. No. 6,113,915.

(F) 6,500,436: filed August 3, 2001 and is a continuation-in-part application of U.S. Ser. No. 09/625,098, filed July 25, 2000, which is a continuation-in-part application of U.S. Ser. No. 09/489,667, filed January 19, 2000.

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Applicant respectfully assert that the Office Action's double patenting rejection is improper. MPEP §706.02(m) states

The practice of rejecting claims on the ground of double patenting in commonly owned applications of different inventive entities is in accordance with existing case law and prevents an organization from obtaining two or more patents with **different expiration dates** covering **nearly identical subject matter**.

(Emphasis added). With regard to comparison of the subject matter, MPEP §804 II B (b) requires a two-way obviousness analysis if the issued patent is filed after the claimed invention. The two-way analysis is an application of the obviousness analysis twice: first determining whether the claimed invention is obvious over the issued claims of the patent, then determining whether the issued claims of the patent is obvious over the claimed invention. If there is non-obviousness either way, then there is no double patenting.

The present double patenting rejection is improper because the claimed invention either has the **same expiration date** as that of the cited patents, or is **not obvious over the claims of the cited patents** (and vice versa).

**I. No Double Patenting Over Patent A.** The present application has the **same expiration date** as that of Patent A. That is, the present application was filed July 16, 2003 and is a divisional of U.S. Ser. No. 08/627,118, filed April 3, 1996, which is a continuation of U.S. Ser. No. 08/173,966, filed December 28, 1993. As such, the present application, once issues, expires on December 28, 2013 (i.e., 20 years from the earliest priority date). This is the same expiration date as Patent A. Thus, a double patenting rejection is not applicable to the claimed invention and Patent A.

**II. No Double Patenting Over Patents B-E.** The claimed invention is not obvious over the claims of Patents B-E (hereinafter "the Patent Claims"). For example, the claimed invention is directed to a method of treating arthritic pain by administering to a muscle. On the other hand, the Patent Claims recite a method of treating pain by intraspinal administration (Patent B, C and D) or intrathecal administration (Patent E),

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which is administering to the central nervous system (CNS).<sup>1</sup> The teaching of administering botulinum toxin to the CNS to treat pain does not make the claimed invention obvious, because the biological effects of administering botulinum toxin to the CNS is significantly different from that of administering to the muscle. For example, when administered to the CNS the botulinum toxin primarily acts on nerve cells to modulate the neuronal communications between neurons in the spinal cord and/or brain. On the other hand, when administered to a muscle, the botulinum toxin primarily acts on motor neurons to modulate the contractility of the muscle. Neuronal communications between neurons in the spinal cord/brain and contractility of muscles are two entirely different biological processes. Accordingly, one of ordinary skill would not be motivated to change from modulating neuronal communications to modulating contractility of muscles to treat pain, much less arthritic pain (none of the Patent Claims teach treatment of arthritic pain). Thus, the claimed invention is not obvious over the Patent Claims.

Because Patents B-E all have filing dates after the earliest priority date of the claimed invention, MPEP §804 II B (b) requires the analysis of whether the Patent Claims are obvious over the claimed invention. Applicant respectfully asserts that the Patent Claims are not obvious over the claimed invention for reasons similar to the above. That is, one of ordinary skill would not be motivated to change from modulating contractility of muscles to treat arthritis pain to modulating neuronal communications to treat pain, because the neuronal communication and contractility of muscles are two significantly different processes.

Since the claimed invention is not obvious over the Patent Claims, and vice versa, the double patenting rejection is improper.

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<sup>1</sup> Intraspinal administration is administering the botulinum toxin within the vertebral canal or spinal cord, and intrathecal administration is administering botulinum toxin within a sheath, for example, cerebrospinal fluid that is contained within the dura mater.

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**III. No Double Patenting Over Patent F.** The claimed invention is not obvious over the claims of Patent F. In fact, the claims of the Patent F teaches away from the claimed invention. For example, the claimed invention recites administering botulinum toxin to a muscle for treating arthritic pain. Thus, it is important for the botulinum toxin of the claimed invention to have a carboxyl heavy chain domain ( $H_c$ ) that can bind to neuromuscular junctions at the site of the injected muscle.<sup>2</sup> On the other hand, the claims of Patent F teaches the use of a modified botulinum toxin for treating pain, wherein the modified botulinum toxin has a no ability, or reduced ability, to bind to neuromuscular junctions. As the claims of Patent F recite, the modified botulinum toxin is

a botulinum toxin covalently coupled to substance P ... the botulinum toxin component compris[ing] both a proteolytic domain and an H chain which comprises an  $H_c$  domain, and wherein the  $H_c$  domain is removed or modified in order to reduce the binding of the botulinum toxin component to receptors at the neuromuscular junction

Clearly, the claimed invention requires that the botulinum toxin be able to bind to neuromuscular junctions; whereas, the claims of Patent F require that the modified botulinum toxin have no or reduced ability to bind to neuromuscular junctions. Thus, the claims of Patent F teaches away from the claimed invention. Accordingly, the claimed invention is not obvious over the claims of Patent F.

Because Patent F has a filing date after the earliest priority date of the claimed invention, MPEP §804 II B (b) requires the analysis of whether the claims of Patent F is obvious over the claimed invention. Applicant respectfully asserts that the claims of Patent F is not obvious over the claimed invention for reasons similar to the above. That is, one of ordinary skill would not be motivated modify the botulinum toxin of the

<sup>2</sup> Page 4 of the specification discloses that botulinum toxin for use in accordance with the present invention may be obtained commercially by establishing and growing cultures of *C. botulinum* in fermenter and then harvesting and purifying the fermented mixture in accordance with known techniques. It is well known that botulinum toxin produced by *C. botulinum* has an  $H_c$  that binds to neuromuscular junctions.

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claimed invention to have no or reduced binding to neuromuscular junctions, because it is important for the claimed invention to employ botulinum toxins that are able to bind to neuromuscular junctions.

Since the claimed invention is not obvious over the claims of Patent F, and vice versa, the double patenting rejection is improper.

**PATENTS B-F CANNOT BE PRIOR ART FOR §103(a) CONSIDERATIONS**

The Office Action indicates that the claims may be rejected for being obvious over Patents B-F. Applicant respectfully reminds the Office that the present application has a priority date of December 28, 1993, which predates the priority dates and issuance dates of Patents B-F (see above). That is, since Patents B-F were filed and published after the priority date of the present application, it cannot be cited as prior art for a rejection under 35 U.S.C. §103(a).<sup>3</sup>

In view of the foregoing, Applicant submits that the pending claims are in condition for allowance, and an early Office Action to that effect is earnestly solicited.

Respectfully submitted,



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<sup>3</sup> The present application is assigned to Allergan. Patents A-F are also assigned to Allergan, as shown on the face of these patents.